PATENT
0230-0236PUS1

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant:	Takeshi IMANISHI et al.	Conf.:	3122
Appl. No.:	10/569,949	Group:	UNKNOWN
Filed:	February 28, 2006	Examiner:	UNKNOWN
For:	NOVEL ARTIFICIAL NUCLEIC ACIDS OF N-O BOND CROSSLINKAGE TYPE		

REQUEST UNDER 37 C.F.R. §1.221(b)

Commissioner for Patents
P.O. BOX 1450
Alexandria, VA 22313-1450

Sir:

Applicants respectfully request that a material mistake made by the Office in the pre-Grant Publication (US Publication No. 2007/0167387 A1) be corrected.

At page 22, paragraph [0214] of US 2007/0167387 [Chemical Formula 8] there are four chemical formulas, and each one of the four formulas at page 22 contains errors as described below:

- each one of the four formulas should have a "T" as the substituent at the top right hand side position of the formula;
- the formula at the bottom of the first column at page 22 of US 2007/0167387, and the second formula in the second column of page 22, each have an error in the representation of the bond connecting the phosphate group to the ring.

A marked up copy of page 22 of US 2007/0167387 is attached. Applicants also attach a copy of page 76 of the specification which correctly shows the four figures.

Applicants submit that the figures provide support under 35 U.S.C. §112, in part, for claim 1. Accordingly, the above described errors constitute a material mistake by the Office. Applicants therefore respectfully request the Office to republish the document under 37 C.F.R. 1.221(b).

Conclusion

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachments: Marked-up copy of page 22 of US 2007/0167387 1.M.K
Copy of page 76 of specification

[0209] As shown in Table 5, the oligonucleotide analogues (6) to (11) and (18) to (21) of the present invention were found to have an excellent triplex-forming capacity. Their sequence selectivity was also superior to that of the natural antisense strand. Thus, they are believed to be very useful for the antigene method as well.

Experimental Example 3

Measurement of Enzyme Resistance

[0210] Natural (DNA oligonucleotide) and nonnatural oligonucleotides shown below were examined for resistance to exonuclease which degrades the oligonucleotide from the 3'-side.

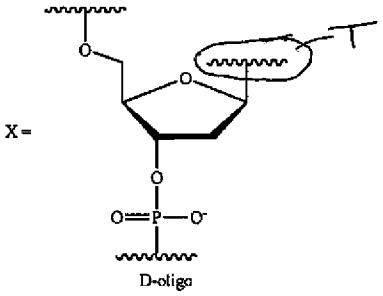
[0211] 1) Each oligonucleotide and snake venom phosphodiesterase (Boehringer Mannheim) as 3'-exonuclease were added, at concentrations of 25 mg/mL and 0.5 mg/mL, into 400 mL of 50 mM Tris-HCl buffer (pH 8.0) containing 10 mM $MgCl_2$, and the mixture was held at 37° C.

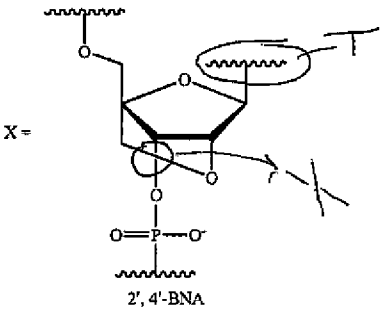
[0212] 2) After a constant period of time, the survival rate of each oligonucleotide was measured by HPLC.

[0213] The sequences of the oligonucleotides used in the measurement are shown below.

[0214] 5'-TTTTTTTTXT-3'

[Chemical Formula 8]





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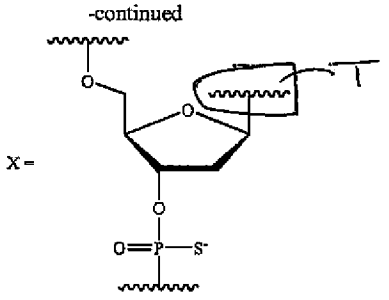

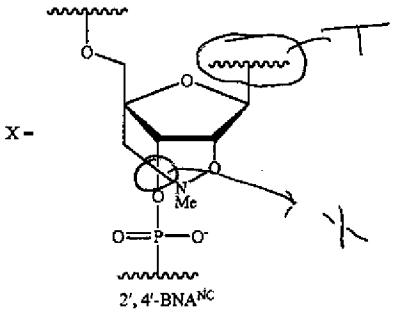

[0215] where when X is a DNA monomer, the oligonucleotide is a completely natural DNA oligonucleotide, and the oligonucleotide containing other nucleotide analogue is a partially nonnatural oligonucleotide; moreover, the oligonucleotide analogue with X being 2',4'-BNA^{NC}(N-Me) is the oligonucleotide analogue of the present invention.

[0216] Changes over time in the survival rates of the respective oligonucleotides, measured by HPLC, are shown in Table 6 and FIG. 1.

[0217] In Table 6 and FIG. 1, "% of intact oligonucleotide" refers to the survival rate (%) (HPLC determination) of the undegraded oligonucleotide at measurement time points to the undegraded oligonucleotide at 0 time point.

TABLE 6

	Evaluation of enzyme resistance					
	% of intact oligonucleotide					
oligonucleotide	0 min	5 min	10 min	20 min	40 min	90 min
D-oligo	100	0	0	0	0	0
2',4'-BNA	100	37	24	5	1	0
S-oligo	100	94	92	91	83	70
2',4'-BNA^{NC}	100	100	99	98	94	80

[0218] The results of Table 6 and FIG. 1 show that the oligonucleotide analogue of the present invention had excellent enzyme resistance as compared with natural and other nonnatural oligonucleotides.

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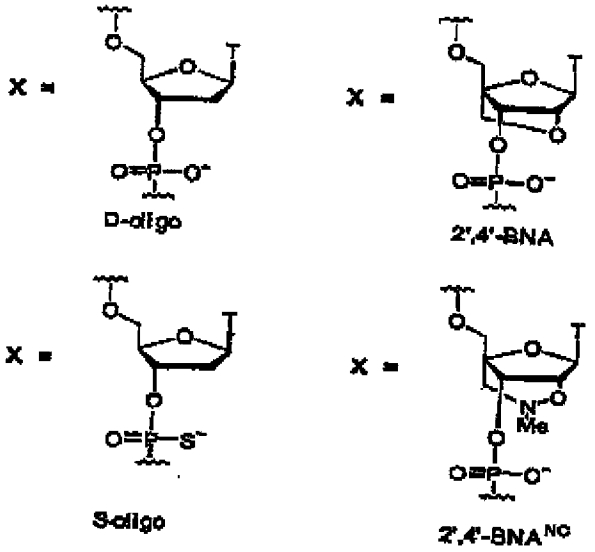

[0148] Where when X is a DNA monomer, the oligonucleotide is a completely natural DNA oligonucleotide, and the oligonucleotide containing other nucleotide analogue is a partially nonnatural oligonucleotide; moreover, the oligonucleotide analogue with X being 2',4'-BNA^{NC}(N-Me) is the oligonucleotide analogue of the present invention.

Changes over time in the survival rates of the respective oligonucleotides, measured by HPLC, are shown in Table 6 and Fig. 1.

[0149] In Table 6 and Fig. 1, "% of intact oligonucleotide" refers to the survival rate (%) (HPLC determination) of the undegraded oligonucleotide at measurement time points to the undegraded oligonucleotide at 0 time point.

[0150] [Table 6]